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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/899,629	07/05/2001	Shuang Liu	N0469.70006US01	5136

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WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
WANG, SHENGJUN	
ART UNIT	PAPER NUMBER
1627	

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05/12/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
09899629	7/5/01	LIU ET AL.	N0469.70006US01

WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
Shengjun Wang	
ART UNIT	**PAPER**
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DATE MAILED:

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Commissioner for Patents

Attached is the supplemental Examiner's Answer, responding to the remend issued by the Board of Patent Appeals and Interferances on August 14, 2007.

/Shengjun Wang/
Primary Examiner, Art Unit 1627

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/899,629
Filing Date: July 05, 2001
Appellant(s): LIU ET AL.

Brian J. Hubbard
For Appellant

Supplemental

EXAMINER'S ANSWER

This is in response to the appeal brief filed October 17 appealing from the Office action mailed January 18, 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is essentially correct. It is noted the subject matter is limited to the elected species of formula I, gallic acid.

Appellants' remarks that Rajopadhy et al. (US 6,537,520) is not a prior art under 35 U.S.C. 103 (c) is persuasive. Therefore, the rejections under 35 U.S.C 103(a) over Rajopadhye et al (US 6537520) in view of Vanderheyden et al. (US 5,679,318) and in further view of Nippon oils (JP 56144060) are herein withdrawn

(7) Claims Appendix

A substantially correct copy of appealed claims 19-22, 30-33, 35-39 appears on pages 32-38 of the Appendix to the appellant's brief. The minor errors are as follows: claims 1-18, 23-29, 34, 40-92 are not appealed claims and should not be in the appendix.

(8) Evidence Relied Upon

The following is a listing of the evidence (e.g., patents, publications, Official Notice, and admitted prior art) relied upon in the rejection of claims under appeal.

US Patent 5,707,603	Toner et al.	January 13, 1998
US Patent 5,750,088	Sworin et al.	May 12, 1998
US 5,679,318	Vanderheyden et al.	October 21, 1997
US 6,537,520	Rajopadhye et al.	March 25, 2003
JP 56-144060 (with English Translation)	Nippon Oils and Fats	November 10, 1981

(9) Grounds of Rejection

Restriction and Species Election

Claims 1-18, 40-92 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, Claims 23-29, 34 are withdrawn from further

consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

1. Applicant's election with traverse of invention group V, claims 19-38. Applicant elected trihydroxy benzoic acid as the stabilizer. Applicant elected RI is 90Y; Ch is chelator; Ln is a linking group; BM is a peptide; and x is 2 as to the radiopharmaceutical compounds, with compound A disclosed at page 68 as a particular example. ***Upon reconsideration, the species election requirement for the radiopharmaceutical compounds regarding to RI, Ch, Ln, BM, and x is herein with drawn*** as the claims are not particularly limited to any species of compounds which comprising a metal chelator linked to a peptide or peptidomimetic, by a linker. The claims have been examined insofar as they read on compounds comprising a metal chelator moiety, a linker, and a peptide or peptidomimetic.

2. Claimed invention. It is noted that the specification defines a "peptide" as "a linear compound having two or more amino acids… that are linked by means of peptide bond." Page 26 of the specification. It is also noted that in illustrating the invention, cyclo-peptide are used as examples See, pages 65-72. Applicants also elected compound A disclosed at page 67 as the peptide compound. Compound A is a cyclo-peptide compound. Further, the claims would read on any other peptidomimetics. The application defines peptidomimetics or pseudopeptide as a compound which mimics the structure of an amino acid residue or a peptide, for example, by using linking groups other than amide linkages between the peptide mimetic and an amino acid residue (pseudopeptide bonds) and/or by using non-amino acid substituents and/or a modified amino acid residue. A pseudopeptide residue means that portion of a pseudopeptide or

peptidomimetic that is present in a peptide. Page 26 of the specification. Therefore, "peptide" or "linear compound" herein is interpretated as read on cyclo-peptide or any peptidomimetics in view of the specification and applicants' election of a cyclo-peptide compound as the "peptide"

3. As an outside matter, it is noted that groups I-IV require the present of (1) a substituted monohydroxyl aromatic compound; (2) a substituted dihydroxyl aromatic compound, in which the two hydroxyl groups are not adjacent to each other; (3) a substituted monohydroxyl-mononmino aromatic compound, in which the hydroxyl group and amino group are not adjacent to each other; or (4) an ortho, meta, or para aminobenzioc acid. See the reasoning of distinct in the restriction requirements mailed December 12, 2002.

Double Patent Rejections

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 19-22, 30-33, 35-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22, 28-30 of U.S. Patent No. 6537520 in view of Vanderheyden et al. (US 5,679,318) and in further view of Nippon oils (JP 56144060).

'520 claims a pharmaceutical composition, or kit, comprising the radionuclide herein. Particularly, the compound A herein disclosed and elected by applicants is claimed. See, claim 30, the compound (r) (column 158, lines 34-36), ^{90}Y is one of the metal claimed. See claim 26. '520 does not expressly claim the stabilizers in the composition or kit. However, Vanderheyden et al. teaches that therapeutical radionuclide compositions generally require the presence of stabilizer. The stabilizer provides enhanced long term stability. One of the well know stabilizer is antioxidant. See, particularly, the abstract. Examples of antioxidants are gentisic acid, or its derivatives, or functionally similar compounds which are suitable for in vivo human administration (column 10, lines 43-58). The amount of stabilizer applied is about 1 mg/ml to 15 mg/ml. (column 10, line 66 to column 11, line 8). The radionuclide may be 90Y (column 5, lines 19-34). Nippon oils teaches gallic acid (3,4,5 trihydroxy benzoic acid, the first trihydroxy benzoic acid recited in claim 22 herein) is a known antioxidant, and are suitable for human consumption. See, particularly, the abstract.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to add antioxidants to the composition in '550 as stabilizers. The employment of the particular antioxidants, e.g., gallic acid and/or gentisic acid is seen to be a selection from amongst equally suitable material and as such obvious, absent evidence to the contrary. Ex parte Winters 11 USPQ 2nd 1387 (at 1388). The employment of more than one antioxidants, e.g., gallic acid and gentisic acid, would have been obvious because it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in

prior art; thus, the claimed invention which is a combination of two known antioxidants sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069.

Claim Rejections 35 U.S.C. 103

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 19-22, 30, 31, 33, 35-39 are rejected under 35 U.S.C. 103(a) as being obvious over Sworin et al. (5,750,088), in view of Vanderheyden et al. (US 5,679,318) and in further view of Nippon oils (JP 56144060).

9. Sworin et al., teaches radionuclide conjugates wherein the radionuclide attached to a biological active groups, i.e., peptide, or protein, (antibody, antibody fragment), or peptidomimetic moiety through a metal chelator moiety. Particularly, Sworin et al. teach a stable

radiopharmaceutical for imaging agent. The compounds comprising a hydrozne (metal chelator) linked to a biological active moiety. The radio active metals include ^{99m}Tc, ^{186}Re, ^{188}Re. See, particularly, the abstract, column 26, line 2 to column 27, line 7, column 37, lines 46-58, and the claims in Sworin et al. The teaching of Sworin et al. meet the limitation of the rediolabeled pharmaceutical agent of the formula (II) RI-Ch-Ln-(BM)x as defined in claim 19, 32, 33, 35-37 herein.

10. The primary references do not teach expressly adding stabilizers, such as gallic acid, in the radionuclide conjugate composition.

11. However, Vanderheyden et al. teaches that therapeutical radionuclide compositions generally require the presence of stabilizer. The stabilizer provides enhanced long-term stability. One of the well know stabilizer is antioxidant. See, particularly, the abstract. Examples of antioxidants are gentisic acid, or its derivatives, or functionally similar compounds which are suitable for in vivo human administration (column 10, lines 43-58). The amount of stabilizer applied is about 1 mg/ml to 15 mg/ml. (column 10, line 66 to column 11, line 8). The radionuclide may be ^{90}Y, ^{186}Re, or ^{188}Re (column 5, lines 19-34). Nippon oils teaches gallic acid (3,4,5 trihydroxy benzoic acid, the first trihydroxy benzoic acid recited in claim 22) is a known antioxidant, and are suitable for human consumption. See, particularly, the abstract.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to add antioxidants to the radionuclide conjugate compositions disclosed in the primary references as stabilizers. The employment of the particular antioxidants, e.g., gallic acid and/or gentisic acid is seen to be a selection from amongst equally suitable material and as such obvious, absent evidence to the contrary. Ex parte Winters 11

USPQ 2nd 1387 (at 1388). The employment of more than one antioxidants, e.g., gallic acid and gentisic acid, would have been obvious because it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus, the claimed invention which is a combination of two known antioxidants sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069.

12. Claims 19-22, 30-33, 35-39 are rejected under 35 U.S.C. 103(a) as being obvious over Toner et al. (US 5,707,603), in view of Vanderheyden et al. (US 5,679,318) and in further view of Nippon oils (JP 56144060).

13. Toner et al. teaches radionuclide conjugates wherein the radionuclide attached to a peptide, or protein, or peptidomimetic moiety through a metal chelator moiety. See the abstract and the claims. Particularly, Toner et al teaches a complex (metal chelator) linked to an immunoreactive group through an amino group, or amino containing moiety. See, e.g., compounds 20-24 in columns 19-22. The radioactive metals include ^{90}Y (claims 15, 21). The immunoreactive group may be peptide, antibody and fragment of antibody, etc. (claim 12). The teaching of Toner et al. meet the limitation of the rediolabeled pharmaceutical agent of the formula (II) RI-Ch-Ln-(BM)x as defined in claim 19, 32, 33, 35-37 herein.

14. The primary references do not teach expressly adding stabilizers, such as gallic acid, in the radionuclide conjugate composition.

15. However, Vanderheyden et al. teaches that therapeutical radionuclide compositions generally require the presence of stabilizer. The stabilizer provides enhanced long-term stability. One of the well know stabilizer is antioxidant. See, particularly, the abstract. Examples of antioxidants are gentisic acid, or its derivatives, or functionally similar compounds which are suitable for in vivo human administration (column 10, lines 43-58). The amount of stabilizer applied is about 1 mg/ml to 15 mg/ml. (column 10, line 66 to column 11, line 8). The radionuclide may be 90Y (column 5, lines 19-34). Nippon oils teaches gallic acid (3,4,5 trihydroxy benzoic acid, the first trihydroxy benzoic acid recited in claim 22) is a known antioxidant, and are suitable for human consumption. See, particularly, the abstract.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to add antioxidants to the radionuclide conjugate compositions disclosed in the primary references as stabilizers. The employment of the particular antioxidants, e.g., gallic acid and/or gentisic acid is seen to be a selection from amongst equally suitable material and as such obvious, absent evidence to the contrary. Ex parte Winters 11 USPQ 2nd 1387 (at 1388). The employment of more than one antioxidants, e.g., gallic acid and gentisic acid, would have been obvious because it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus, the claimed invention which is a combination of two known antioxidants sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069.

Response to the Arguments

Appellants argue that the double Patenting rejections over '520 are improper because references other than the '520 patent were cited in the rejections. The arguments have been fully considered, but are not persuasive. It should be understood that secondary references are permissible in the double patenting rejections. See, MPEP 8.04.

16. In response to appellants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Particularly, Vanderheyden et al. teach a specific dihydroxy benzoic acid, and its derivatives or functionally similar compounds, for use as antioxidants. The teaching would have fairly suggested that trihydroxy benzoic acid would be similarly useful. Nippon Oil and Fats is cited to show the trihydroxy benzoic acid is a known antioxidant in the art. Therefore, considering the cited references as a whole, the employment of trihydroxy benzoic acid as a stabilizer in radioactive therapeutical composition would have been obvious to one of ordinary skill in the art. The examiner has noted that appellant meticulously excluded the compounds particularly disclosed by Vanderheyden et al. from the claimed antioxidants herein. Such negative limitations are sufficient to avoid a clear anticipation by the prior art, but are not persuasive to the obvious rejections set forth above. The scope of antioxidants suggested by Vanderheyden et al. is much larger than those three specific compounds. Vanderheyden et al. teach the stabilizers used in radioactive composition include antioxidants and challenging agents which are suitable for in vivo human administration, such as ascorbic acid, gentisic acid, reductic acid, *and their derivatives, and functionally similar*

compounds. (col. 10, line 43-50). In view of the teaching by Vanderheyden et al, and the fact that gallic acid is a structural derivative of gentisic acid (with one more hydroxyl group at the aromatic ring), and is a known antioxidant, one of ordinary skill in the art would have seen the employment of gallic acid in a radio active composition as an obvious variation to gentisic acid. Further, there is no evidence on the record showing the antioxidants herein recited are any different functionally from those disclosed by Vanderheyden et al.

In response to appellants' arguments that Nippon Oil and Fats is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Nippon oil is reasonably pertinent to the particular problem with which the applicant was concerned, i.e., non-toxic antioxidant suitable for human consumption.

Appellants further contend that Nippon Oils and Fats requires the combination of ascorbic acid and gentisic acid, and therefore, teach away from the instant claims.

The arguments have been fully considered but are not persuasive. It is noted that the features upon which applicant relies (i.e., no combination with ascorbic acid) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, the rejections are based on the combination of the cited references, Nippon oil was cited to show that the trihydroxy benzoic acid recited herein is known in the art as an antioxidant.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Particularly, appellants contend that

"the Toner reference discloses that not all antioxidants work equally well in pharmaceuticals in the Background section, which explains that choosing the identity of the antioxidant is critical:

Another problem with some prior art compositions is that the chelator must be activated by a reducing agent before forming the radionuclide chelate. If the protein conjugates are to be formed prior to formation of the radionuclide chelate, then the reducing agent employed for activating the complexing agent can degrade the protein."

Thus, the teachings of record strongly rebut the implication that antioxidants are interchangeable. The Examiner is impermissibly using hindsight based on Appellant's disclosure."

The arguments are not persuasive. First, the citation from Toner reference is about the timing of contacting radionuclide by the chelator, not about the kind of antioxidant being added to the radionuclide composition. Second, the trihydroxyl benzoic acid herein is not any other antioxidant, but a structurally related, and is known to be suitable for human in vivo administration.

17. As to the rejections under 35 U.S.C. 103(a) over Sworin et al. (5,750,088), in view of Vanderheyden et al. (US 5,679,318) and in further view of Nippon oils (JP 56144060), appellants do not dispute that Sworin et al. teach the radionuclide conjugates herein, but argue that the cited references fails to provide sufficient teaching or suggestion to use the particular trihydroxyl benzoic acid, Gallic acid. Particularly appellants argue that Sworin et al. fails to teach any compound of formula I.

18. In response to appellants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Particularly, Vanderheyden et al. teach a specific dihydroxy benzoic acid, and its derivatives or functionally similar compounds, for use as antioxidants. The teaching would have fairly suggested that trihydroxy benzoic acid would be similarly useful. Nippon Oil and Fats is cited to show the trihydroxy benzoic acid is a known antioxidant in the art. Therefore, considering the cited references as a whole, the employment of trihydroxy benzoic acid as a stabilizer in radioactive therapeutical composition would have been obvious to one of ordinary skill in the art. The examiner has noted that appellant meticulously excluded the compounds particularly disclosed by Vanderheyden et al. from the claimed antioxidants herein. Such negative limitations are sufficient to avoid a clear anticipation by the prior art, but are not persuasive to the obvious rejections set forth above. The scope of antioxidants suggested by Vanderheyden et al. is much larger than those three specific compounds. Vanderheyden et al. teach the stabilizers used in radioactive composition include antioxidants and challenging agents, which are suitable for in vivo human administration, such as

ascorbic acid, gentisic acid, reductic acid, *and their derivatives, and functionally similar compounds*. (col. 10, line 43-50). In view of the teaching by Vanderheyden et al, and the fact that gallic acid is a structural derivative of gentisic acid (with one more hydroxyl group at the aromatic ring), and is a known antioxidant, one of ordinary skill in the art would have seen the employment of gallic acid in a radio active composition as an obvious variation to gentisic acid. Further, there is no evidence on the record showing the antioxidants herein recited are any different functionally from those disclosed by Vanderheyden et al.

Appellants' remarks about Yoshinaga are not persuasive for reasons set for above.

19. As to the rejections under 35 U.S.C. 103(a) over Toner et al. (5,707,603), in view of Vanderheyden et al. (US 5,679,318) and in further view of Nippon oils (JP 56144060), appellants do not dispute that Sworin et al. teach the radionuclide conjugates herein, but argue that the cited references fails to provide sufficient teaching or suggestion to use the particular trihydroxyl benzoic acid, Gallic acid. Particularly appellants argue that Sworin et al. fails to teach any compound of formula I. For similar reasons as set forth above, the arguments are not persuasive.

20. Particularly, Vanderheyden et al. teach a specific dihydroxy benzoic acid, and its derivatives or functionally similar compounds, for use as antioxidants. The teaching would have fairly suggested that trihydroxy benzoic acid would be similarly useful. Nippon Oil and Fats is cited to show the trihydroxy benzoic acid is a known antioxidant in the art. Therefore, considering the cited references as a whole, the employment of trihydroxy benzoic acid as a stabilizer in radioactive therapeutical composition would have been obvious to one of ordinary skill in the art. The examiner has noted that appellant meticulously excluded the compounds

particularly disclosed by Vanderheyden et al. from the claimed antioxidants herein. Such negative limitations are sufficient to avoid a clear anticipation by the prior art, but are not persuasive to the obvious rejections set forth above. The scope of antioxidants suggested by Vanderheyden et al. is much larger than those three specific compounds. Vanderheyden et al. teach the stabilizers used in radioactive composition include antioxidants and challenging agents which are suitable for in vivo human administration, such as ascorbic acid, gentisic acid, reductic acid, *and their derivatives, and functionally similar compounds*. (col. 10, line 43-50). In view of the teaching by Vanderheyden et al, and the fact that gallic acid is a structural derivative of gentisic acid (with one more hydroxyl group at the aromatic ring), and is a known antioxidant, one of ordinary skill in the art would have seen the employment of gallic acid in a radio active composition as an obvious variation to gentisic acid. Further, there is no evidence on the record showing the antioxidants herein recited are any different functionally from those disclosed by Vanderheyden et al.

In response to appellants' arguments that Nippon Oil and Fats is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Nippon oil is reasonably pertinent to the particular problem with which the applicant was concerned, i.e., non-toxic antioxidant suitable for human consumption.

Appellants further contend that Nippon Oils and Fats requires the combination of ascorbic acid and gentisic acid, and therefore, teach away from the instant claims.

The arguments have been fully considered but are not persuasive. It is noted that the features upon which applicant relies (i.e., no combination with ascorbic acid) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, the rejections are based on the combination of the cited references, Nippon oil was cited to show that the trihydroxy benzoic acid recited herein is known in the art as an antioxidant.

21. ***Limitations recited in the dependent claims 20-22, 30, 31, 33, 35-39 do not render the claims distinct or unobvious over the cited prior art.*** Particularly, claims 20-22 further require that the stabilizer be trihydroxybenzoic acid, such limitations have been fully disclosed by Nippon oil. Claims 33, 35-37 further define the bioactive molecular as peptide, peptidomimetic, antibody and antibody fragment respectively. Such limitation have been fully disclosed or suggested by Sworin et al., Toner et al. Claim 38 further required a second stabilizer, which read on gentisic acid, which is disclosed by Vanderheyden et al. Claims 30 and 39 define the amount of the stabilizer(s). The selection of the optimal amount of a functional agent in a pharmaceutical composition is a matter of optimization of result affecting parameters, which is considered within the skill of artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215. In instant case, it would have been obvious, particularly in view of the disclosure of Vanderheyden et al. regarding the amount of stabilizer employed in the composition. Claim 31 recite the level of radioactivity. Such activity is deemed to be a result affecting parameter and the optimization of such level would have been considered within the skill of the artisan. See, e.g., column 37, lines 46-58 in

Sworin et al. Claim 32 require the radioisotope be ^{90}Y, which is disclosed in Toner et al. and Vanderheyden et al.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Shengjun Wang/

Primary Examiner, Art Unit 1627

Conferees:

Sreeni Padmanabhan Michael Hartley